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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/445,614	12/08/1999	Timothy Peter Bonnert	T1481	1165

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Patent Department
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EXAMINER
BRANNOCK, MICHAEL T

ART UNIT	PAPER NUMBER
1646	

DATE MAILED: 11/23/2001

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/445,614	Bonnert, Timothy P.	
	Examiner	Art Unit	
	Michael T Brannock	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period f r Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 March 2001* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3,5-10,12,13,15 and 16* is/are pending in the application.

4a) Of the above claim(s) *6,10,12,13,15 and 16* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *1,3,5 and 7-9* is/are rejected.

7)☐ Claim(s) *2* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☒ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: *See Continuation Sheet* .

Continuation of Attachment(s) 6). Other: Notice to comply with sequence rules.

DETAILED ACTION

Status of Application: Claims and Amendments

Applicant is notified that the amendments put forth in Paper 6, 12/8/99, have been entered in full. Claims 1-3, 5-10, 12, 13, 15, 16 are pending.

Claims 6, 10, 12, 13, 15, 16 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 9, 3/28/01. The traversal is on the grounds that a search of Groups I-IV would not be a serious burden on the examiner and that a thorough search of any one of the groups would constitute a sufficient search to evaluate all the claims of the present application. This is not found persuasive for the following reasons:

Under MPEP § 803, there are two criteria for a proper requirement for restriction between patently distinct inventions:

(A) The inventions must be independent (see MPEP § 8702.01, 806.04, 808.01) or distinct as claimed (see MPEP § 806.05- §806.05(I)): and
(B) There must be a serious burden on the examiner if restriction is required (see MPEP § 803.02, § 806.04(a)- 806.04(I), § 808.01(a), and § 808.02).

Consistent with current patent practice, a serious search burden may be established by (A) separate classification thereof: (B) a separate status in the art when they are classifiable together: (C) a different field of search. These criteria were met in the above restriction. Further, a search is directed not only to art which would be anticipatory, but also to art that would render the invention obvious. In the instant case, for example, although a search of the polypeptides of Group III would overlap a search of the polynucleotides of Group I, the two

searches would not be coextensive. In many instances, a protein will have been known in the art before the DNA has been discovered that encodes the protein. Often the protein will be known by a name different than the name given the protein after the cloning of the nucleic acid - and may even be associated with a completely different activity than that ascribed to it when the nucleic acid was cloned. Although a search of any one of the Groups I-IV may overlap that of another, the search of one group could not be relied upon, solely, to provide art that is anticipatory or would render obvious the invention of any other group. Thus, Groups I-IV require divergent searches, and to search all inventions would be burdensome. Therefore, the restriction is maintained and made final.

Priority

Acknowledgment is made of applicant's claim for foreign priority based on an application filed in the United Kingdom on 12/8/1998. It is noted, however, that applicant has not filed a certified copy of the foreign application as required by 35 U.S.C. 119(b).

Sequence Rules Compliance:

This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2), see page 16 of the specification for example. However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the reason(s) set forth on the attached Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence and/or Amino Acid Sequence Disclosures. The instant SEQ ID NO: 2 comprises a region of approximately 60 residues beginning at position 89 that consists of amino acids whose single

letter abbreviation is either A, T, C, or G. Thus, it is likely that a nucleic acid sequence was inadvertently incorporated into SEQ ID NO: 2.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claim 1 is rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. The claim does not require that the claimed complement of a polynucleotide encoding a polypeptide of SEQ ID NO: 2 be isolated (e.g. recombinant), thus the claim encompasses the noncoding strand of a human chromosome encoding the protein of SEQ ID NO: 2, present in a human being, and as such is not patentable

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 2 and 5 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 2 requires "a portion thereof". It is unclear if this phrase refers to the complement of the polynucleotide or the polynucleotide itself or both; therefore the metes and bounds of the claim cannot be determined.

Claim 5 requires a probe comprising an oligomer specific to the polynucleotide of claim 2. The phrase "specific to" renders the claims indefinite because this phrase is known in the art to be a relative term and in the context of the instant claim could mean "exclusive to" or any lesser unspecified degree of specificity. There appears to be no definition of term in the specification that clearly sets forth a way to determine what is and what is not "specific to". Thus, the metes and bounds of the claim cannot be determined.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 3 and 5 rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for polynucleotides encoding a polypeptide of SEQ ID NO: 2, and for polynucleotides *consisting* of a fragment of said polynucleotides, and for polynucleotides *consisting of* said fragments *and* a heterologous polynucleotide (e.g. vector), does not reasonably provide ennoblement for polynucleotides *comprising* a portion of said polynucleotides wherein the polynculeotide is other than that encoding SEQ ID NO: 2. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

It is noted that claim 5 does not require that the probe be specific to the polynucleotide of claim 2, only that the *oligomer* is specific to the polynucleotide of claim 2. There is no size limitation to the oligomer. The claims encompass polynucleotides encoding polypeptide variants of the polypeptide of SEQ ID NO: 2, i.e. substitutions, deletions or insertions in a protein corresponding to SEQ ID NO: 2; yet Applicant has not provided sufficient guidance as to how to make and use the encoded polypeptides which are not identical to the polypeptide of SEQ ID NO: 2, but which still retain a desired property of the polypeptide of SEQ ID NO: 2. The specification has failed to teach one of skill in the art which amino acid substitutions, deletions or insertions to make. Furthermore, the Applicant has not provided guidance as to what properties of the encompassed allelic variants or other sequence variants of the protein corresponding to SEQ ID NO: 2 might be desired nor any guidance as to which amino acid substitutions, deletions or insertions to make to achieve any desired property. Applicant has not defined a difference in structure or difference in function between the protein corresponding to SEQ ID NO: 2 and variants of said protein. If a variant of the protein corresponding to SEQ ID NO: 2 is to have a structure and function similar to the protein corresponding to SEQ ID NO: 2, then the specification has failed to teach one of skill in the art which amino acid substitutions, deletions or insertions to make that will preserve the structure and function of the protein corresponding to SEQ ID NO: 2.

The problem of predicting protein structure from sequence data and in turn utilizing predicted structural determinations to ascertain functional aspects of the protein is extremely complex. While it is known that many amino acid substitutions are generally possible in any given protein, the positions within the protein's sequence where such amino acid substitutions

can be made with a reasonable expectation of success are limited. Certain positions in the sequence are critical to the protein's structure/function relationship, e.g. such as various sites or regions directly involved in binding, activity and in providing the correct three-dimensional spatial orientation of binding and active sites. These or other regions may also be critical determinants of antigenicity. These regions can tolerate only relatively conservative substitutions or no substitutions (see Bowie et al., 1990, Science 247:1306-1310, especially p.1306, column 2, paragraph 2). However, Applicant has provided little or no guidance beyond the mere presentation of sequence data to enable one of ordinary skill in the art to determine, without undue experimentation, the positions in the protein which are tolerant to change (e.g. such as by amino acid substitutions or deletions), and the nature and extent of changes that can be made in these positions. Although the specification outlines art-recognized procedures for producing and screening for active muteins, this is not adequate guidance as to the nature of active variants that may be constructed, but is merely an invitation to the artisan to use the current invention as a starting point for further experimentation. Even if an active or binding site were identified in the specification, they may not be sufficient, as the ordinary artisan would immediately recognize that an active or binding site must assume the proper three-dimensional configuration to be active, which conformation is dependent upon surrounding residues; therefore substitution of non-essential residues can often destroy activity.

Due to the large quantity of experimentation necessary to generate the infinite number of variants required by the claims and possibly screen same for activity, the lack of direction/guidance presented in the specification regarding which structural features are required in order to provide activity, the absence of working examples directed to same, the complex

nature of the invention, the state of the prior art which establishes the unpredictability of the effects of mutation on protein structure and function, and the breadth of the claims which fail to recite any structural or functional limitations, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope.

Claims 3 and 5 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The specification discloses a polynucleotide of SEQ ID NO: 1, yet the claims encompass polynucleotides not described in the specification, e.g., sequences from other species, mutated sequences, allelic variants, or sequences that have a recited degree of identity. None of these sequences meet the written description provision of 35 U.S.C. 112, first paragraph. Although one of skill in the art would reasonably predict that these sequences exist, one would not be able make useful predictions as to the nucleotide positions or identities of those sequences based on the information disclosed in the specification.

A genus claim may be supported by a representative number of species as set forth in Regents of the University of California v Eli Lilly & Co, 119F3d 1559, 1569, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997). A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus, or of a recitation of structural features common to the genus, which features constitute a substantial portion of the genus. The instant specification discloses,

however, a single isolated polynucleotide sequence SEQ ID NO: 1 . No activity is set forth for the additional sequences encompassed by the claims. Further, even if the disclose sequence were definitive of a genus with a specified function, the instantly claimed genus is not so limited and the prior art does not provide compensatory structural or correlative teachings to enable one of skill to identify/obtain the polynucleotides encompassed.

With the exception of the of the polynucleotide of SEQ ID NO: 1, the skilled artisan cannot envision the detailed chemical structure of the encompassed variants. Therefore, only the polynucleotide of SEQ ID NO: 1, and polynucleotides consisting of fragments thereof or comprising said fragments and a heterologous sequence (e.g. vector), but not the full breadth of the claims meet the written description provision of 35 U.S.C. §112, first paragraph.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

Claims 1, 3, 5, 7, 8, 9 are rejected under 35 U.S.C. 102(a) as being anticipated by Caterina et al. Nature 398(436-441), April 20, 1999. Caterina et al. disclose polynucleotides comprising the coding region of the polynucleotide of SEQ ID NO: 1 (see attached sequence

alignment), probes specific to said polynucleotide and methods of making a polypeptide (see Methods).

Claims 3 and 5 are rejected under 35 U.S.C. 102(e) as being anticipated by US Patent 5834183. The claims require a portion of a polynucleotide of SEQ ID NO: 1, or a probe comprising and oligomer that is specific to SEQ ID NO: 1. US Patent 5834183 (SEQ ID NO: 7) disclose a polynucleotide comprising a portion of SEQ ID NO: 1 (see attached sequence alignment). US Patent 5834183 disclose that the polynucleotide can be used as a probe (e.g. see col 12).

Claim 3 is rejected under 35 U.S.C. 102(b) as being anticipated by the SIGMA Product Catalogue, 1992. The claims require a portion of a polynucleotide of SEQ ID NO: 1. The raw sequence listing indicates that the sequence AAA is located beginning at position 2000 of SEQ ID NO: 1. The SIGMA Product catalogue discloses oligodeoxyadenylic acid consisting of AAA, see page 743 product O 4253.

Allowable Subject Matter

Claim 2 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Conclusion

No claims are allowable

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michael Brannock, Ph.D., whose telephone number is (703) 306-5876. The examiner can normally be reached on Mondays through Thursdays from 8:00 a.m. to 5:30 p.m. The examiner can also normally be reached on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler, Ph.D., can be reached at (703) 308-6564.

Official papers filed by fax should be directed to (703) 308-4242. Faxed draft or informal communications with the examiner should be directed to (703) 308-0294.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

YVONNE EYLER, PH.D
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600